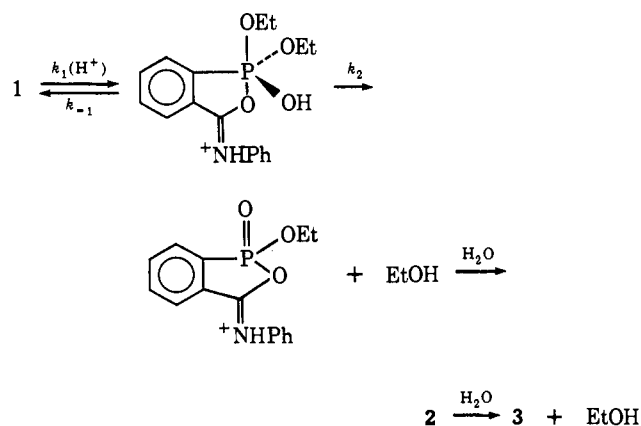


considerations is presented in Scheme I. A pentacoordinate hydrolysis intermediate is indicated and has

Scheme I



been configured in a manner consistent with known energetics.<sup>19</sup> Pseudorotation of pentacoordinate intermediates is prohibited by steric and electronic requirements of the phosphonate ring system.<sup>20,21</sup> The involvement of such intermediates is not obligatory since products of the reaction must arise from "in line displacements"<sup>22</sup> as shown in Scheme I in which distinction between intermediate and transition state is not readily discernible. Cyclic tetracoordinate intermediates can react with water only to give ring-opened products in any case (and not alcohol). The rate expression corresponding to Scheme I and consistent with the data in Figure 1, where  $k_2$  is the rate constant of the rate-determining step, is

$$\frac{d[2\text{EtOH}]}{dt} = \frac{k_1 k_2 [1][H^+]}{k_{-1} + k_2} \quad (1)$$

$$k_{\text{obsd}} = \frac{k_1 k_2 [H^+]}{k_{-1} + k_2}$$

Our data indicate that amide phosphorylation can occur in properly constituted systems (in a manner similar to that proposed for peptide participation in acyl transfer reactions<sup>23</sup>). A phosphorylated peptide linkage could be an intermediate in enzymatic phosphate transfer and hydrolysis reactions. Phosphorylation of a peptide bond could lead to a change of conformation of the protein, since the geometry of that peptide should be quite different from that of a normal peptide bond. In the reverse reaction, conformational change of a protein could lead *via* addition of phosphate to peptide linkages to products associated with oxidative phosphorylation.<sup>24</sup> We are continuing our studies on the phosphorylation of amides and re-

lated compounds in order to obtain data that will assist in the detection of such intermediates.

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Ronald Kluger,\* Joseph L. W. Chan

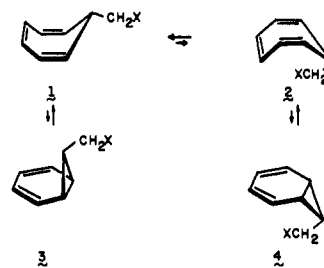
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### On the Absence of Significant Remote $\pi$ -Bond Effects during Solvolysis of Epimeric Annulated 7-Cycloheptatrienylmethyl 3,5-Dinitrobenzoates<sup>1</sup>

Sir:

Sargent and his coworkers have drawn attention to the interesting fact that the solvolysis of 7-cycloheptatrienylmethyl 3,5-dinitrobenzoate proceeds by prior isomerization to the norcaradienylcarbinyl valence tautomer.<sup>2</sup> However, because the configuration of the ionizing molecule could not be determined, the following important factor was not considered in the earlier work. Cycloheptatriene is recognized to exist as a rapidly equilibrating pair of boat conformations ( $E_{\text{act}} \approx 6$  kcal/mol)<sup>3</sup> which comprises a nondegenerate process for many substituted derivatives (e.g.,  $1 \rightleftharpoons 2$ ). Since each of these conformers in turn exists in equilibrium with the corresponding bicyclic form, ionization could conceivably occur from thermodynamically more stable isomer 3 (by virtue of fewer nonbonded interactions), from that isomer (4) in which the incipient



electron-deficient center is nearer the  $\pi$  system (particularly if enhanced stabilization resulted from this interaction), or from both forms at roughly competitive rates should any special effects be absent or fortuitously cancelling.

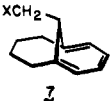
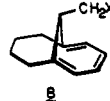
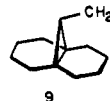
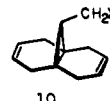
(1) These results were disclosed initially at the 165th National Meeting of the American Chemical Society, New York, N. Y., Sept 1972, No. ORGN 132.

(2) G. D. Sargent, N. Lowry, and S. D. Reich, *J. Amer. Chem. Soc.*, **89**, 5985 (1967).

(3) For a recent review of this subject, see G. Maier, *Angew. Chem., Int. Ed. Engl.*, **6**, 402 (1967).

- (18) C. J. M. Stirling, *J. Chem. Soc.*, 255 (1960).  
 (19) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968).  
 (20) E. A. Dennis and F. H. Westheimer, *J. Amer. Chem. Soc.*, **88**, 3432 (1966).  
 (21) D. S. Frank and D. A. Usher, *J. Amer. Chem. Soc.*, **89**, 6360 (1967).  
 (22) D. A. Usher, *Proc. Nat. Acad. Sci. U. S.*, **62**, 661 (1969).  
 (23) M. L. Bender, G. R. Schonbaum, and G. A. Hamilton, *J. Polym. Sci.*, **49**, 75 (1961).  
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Table I. Solvolysis Data for 3,5-Dinitrobenzoates in 80:20 Acetone-Water

Compound	$T, ^\circ\text{C}^a$	$k, \text{sec}^{-1}{}^b$	$k_{\text{rel}}{}^{100^\circ}$	$\Delta H^\ddagger,$ kcal/mol	$\Delta S^\ddagger,$ eu
 7	69.6	$5.11 \times 10^{-6}$	4.1	27.6	-2.58
	84.4	$3.01 \times 10^{-5}$			
	99.5	$1.41 \times 10^{-4}$			
	100.0 <sup>c</sup>	$1.52 \times 10^{-4}$			
 8	84.3	$8.72 \times 10^{-6}$	1.2	27.1	-6.37
	99.4	$4.12 \times 10^{-5}$			
	100.0 <sup>c</sup>	$4.44 \times 10^{-5}$			
	114.9	$1.89 \times 10^{-4}$			
 9	69.6	$1.63 \times 10^{-5}$	10	25.6	-5.95
	84.3	$8.02 \times 10^{-5}$			
	99.5	$3.59 \times 10^{-4}$			
	100.0 <sup>c</sup>	$3.77 \times 10^{-4}$			
 10	84.3	$6.78 \times 10^{-6}$	1.0	28.2	-3.78
	99.5	$3.64 \times 10^{-5}$			
	100.0 <sup>c</sup>	$3.75 \times 10^{-5}$			
	114.8	$1.64 \times 10^{-4}$			

<sup>a</sup>  $\pm 0.1^\circ$ . <sup>b</sup> Average value from duplicate kinetic runs. The reproducibility was very good. <sup>c</sup> Extrapolated or interpolated values based upon thermodynamic parameters.

It was of interest to resolve this dilemma, and the unsaturated 11-substituted bicyclo[4.4.1]undecanes **7**, **8**, and **11** were therefore synthesized.<sup>4</sup> Since the bridging of C<sub>1</sub> to C<sub>6</sub> with a tetramethylene chain effectively isolates the two conformers, a unique opportunity for investigating the effect of leaving group orientation upon the rates of solvolysis of epimeric 7-cycloheptatrienylmethyl derivatives was at hand. Introduction of a tetramethylene bridge in this fashion has been shown by Vogel not to alter the equilibrium  $5 \rightleftharpoons 6$



to the extent that **6** can be detected by nmr methods.<sup>5</sup> It might be assumed, however, that the free energy difference between **5** and **6** has been decreased significantly relative to the cycloheptatriene-norcaradiene pair since the bracketing effect in the next lower homolog drives the equilibrium totally (nmr analysis) in the tricyclic direction.<sup>5</sup> Quite the converse was expected for **11** where the aromatic character of its 1,6-methano-[10]annulene nucleus was expected to deter valence isomerization to the norcaradienyl counterpart.

The solvolytic data for **7**, **8**, and two suitable reference molecules (**9** and **10**)<sup>4</sup> in 80% (vol) acetone-water are summarized in Table I. The insolubility of **11** in this solvent system (or any other reasonable aqueous acetone combination) required the use of a nonaqueous medium, and tetrahydrofuran-methanol (75:25) was therefore employed. Under these conditions, however,

(4) Details of our synthetic approaches will appear in the full paper on this subject. Elemental analyses on all intermediates and final products were satisfactory and spectra (nmr, ir, uv, mass) were compatible in all instances.

(5) E. Vogel, W. Weidemann, H. Kiefer, and W. F. Harrison, *Tetrahedron Lett.*, 673 (1963).

transesterification was a significant reaction pathway (see equation).<sup>6</sup>

The spread of relative rate constants at 100° for **7**–**10** is seen to consist of only a tenfold difference between the extremes. Indeed, these data serve to support additionally the Sargent proposal that such reactions of 7-cycloheptatrienylmethyl derivatives proceed by cyclopropyl-assisted ionization. The tenfold rate decrease observed for **10** relative to **9** is fully in agreement with the factor estimated for the inductive contribution of two  $\beta$ -oriented double bonds.<sup>2,7</sup>

When the kinetic behavior of **7** and **8** is compared, it becomes evident that rigid orientation of the developing positive charge directly above the center of the 1,3-diene moiety in **8** promotes little or no overt rate effect not available also to the anti isomer **7**.<sup>8</sup> The latter dinitrobenzoate is seen to exhibit a 3.4-fold rate enhancement relative to **8**. The absence of interaction with the diene unit was anticipated to some extent, since to achieve maximum conjugation with the bent side bonds of the three-membered ring, the developing p orbital must assume an orthogonal relationship to the  $\pi$  system as in **12**. But why through-space effects are not more in evidence is still an open question and must await further work in allied systems. Perhaps the

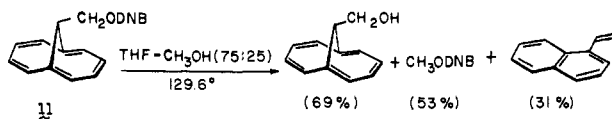
(6) In actuality, dinitrobenzoate **11** does undergo competing alkyl-oxygen ionization to a limited extent with the formation of alcohol of unrearranged structure. At 100°, no 1-vinylnaphthalene is in evidence, but at 130° this hydrocarbon is formed in 31% yield (results of W. E. Heyd). First-order kinetic behavior was observed ( $k_{128.6^\circ} = 3.38 \times 10^{-5} \text{ sec}^{-1}$ ). Since the rate of acid production from **8** under these conditions was  $8.48 \times 10^{-5} \text{ sec}^{-1}$ , only a small (2.5-fold) kinetic factor apparently separates these two systems.

(7) E. N. Peters and H. C. Brown, *J. Amer. Chem. Soc.*, **94**, 5899 (1972); C. F. Wilcox, Jr., and H. D. Banks, *ibid.*, **94**, 8231 (1972); H. Tanida and T. Irie, *J. Org. Chem.*, **36**, 2777 (1971).

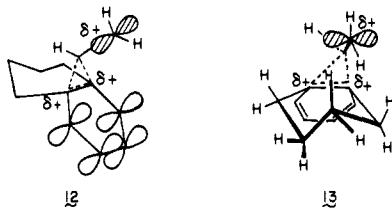
(8) Preliminary product studies with **7** and **8** point to the formation of 1-vinylnaphthalene as the principal, if not exclusive, solvolysis product. This aromatic is presently considered to arise from cyclopropane edge bond rupture in the respective norcaradienyl valence tautomers, 1,2-vinyl shift in the resulting cyclohexadienyl cation, and ultimate deprotonation.

structural features inherent in **12** position both p orbital lobes of the electron-deficient carbon atom sufficiently distant from those of the diene component that *measurable* interaction does not operate.

Since the solvolyses of **7**, **8**, and **11** appear dependent



upon the operation of a preequilibrium, the observed rate constants comprise in reality a composite of pseudo-first-order rate and equilibrium constants ( $k_{\text{obsd}} = k_1 K_{\text{eq}}$ ). However, it is not imperative to invoke differences in  $K_{\text{eq}}$  to account for the somewhat more rapid ionization of **7** relative to **8**. A careful study of molecular models reveals that the carbinyl centers in **7** and its tricyclic valence tautomer experience steric compression with the axially disposed hydrogen atoms of the tetramethylene bridge (*cf.* **13**). Similar interactions



are absent in **8**. To maintain maximum orbital overlap, one hydrogen atom bonded to the carbinyl carbon must be positioned directly in the center of a cluster of ring protons. This nonbonded repulsion may be relieved by the development of some homoallylic character which gives rise to dissymmetric features as in **13**. In contrast, **12** could be a more symmetric ion. Interestingly, these conclusions are compatible with the observed differences in the relevant entropies of activation.

The present solvolyses denote that the large cyclopropyl-assisted rate accelerations available to **1** and **2** owing to their capacity for facile preisomerization to the norcaradienylcarbinyl derivatives **3** and **4**, respectively, are more than adequate to dampen kinetic effects of lesser magnitude. We therefore conclude that the influence of conformation upon the *rates* of solvolysis of 7-cycloheptatrienylmethanol derivatives is of sufficiently small order not to be an important factor *per se* (*i.e.*,  $k_1(\mathbf{3}) \approx k_1(\mathbf{4})$ ). Acceptance of this latter proposal then requires, of course, that the magnitudes of the relevant preequilibria ( $\mathbf{1} \rightleftharpoons \mathbf{2}$ ;  $\mathbf{1} \rightleftharpoons \mathbf{3}$ ;  $\mathbf{2} \rightleftharpoons \mathbf{4}$ ) control whether **3** or **4** is the predominant reaction species during the ionization of 7-cycloheptatrienylmethyl 3,5-dinitrobenzoate (Curtin-Hammett considerations.)

**Acknowledgment.** The partial financial support of the National Cancer Institute (Grant CA 12115) is acknowledged with gratitude.

(9) Phillips Petroleum Fellow, 1970-1971; University Dissertation Fellow, 1971-1972.

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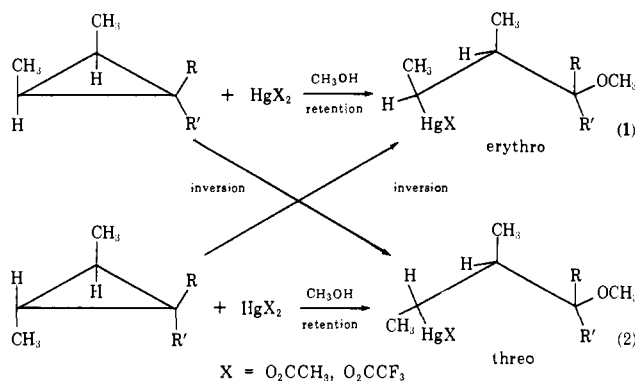
Received December 22, 1972

## Stereochemistry of the Electrophilic Addition of Mercuric Acetates to Cyclopropanes

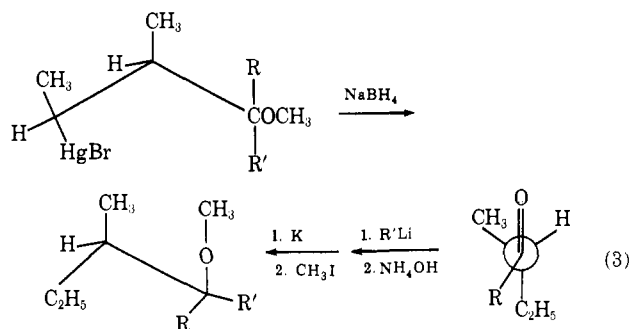
Sir:

The stereochemistry of the reaction of cyclopropanes with various electrophiles has been the subject of a number of investigations, but no general mechanistic pattern has appeared. Thus while cyclopropanes have been shown to react with protons mainly with retention of configuration at the carbon undergoing electrophilic substitution,<sup>1</sup> some examples of inversion are known.<sup>2</sup> Cyclopropanes have been cleaved with mercuric salts with inversion<sup>3</sup> and with positive halogen with inversion<sup>4</sup> and retention.<sup>5</sup> We wish to report the results of a comprehensive study of the reaction of a number of simple cyclopropanes with mercuric acetate and trifluoroacetate in methanol which shows that (1) the stereochemistry of the reaction of the electrophile is generally determined by its attack on the least substituted bond of the ring, (2) the nucleophile reacts almost exclusively with inversion, and (3) in a completely symmetrical system where all ring bonds are identical, inversion predominates slightly in the electrophilic attack.

The reactions whose stereochemistry was studied are shown in eq 1 and 2. The stereochemistry of the prod-



ucts was determined by replacement of the organomercurial with bromine in pyridine under conditions which give exclusively retention of configuration, followed by anti elimination to *cis* and *trans* alkenes from the erythro and threo isomer, respectively.<sup>3</sup> The alkenes in turn were synthesized from previously reported<sup>3</sup> compounds of known structure. The stereochemistry of the methoxyl group was determined by removal of the mercury



- (1) C. H. DePuy, *Accounts Chem. Res.*, **1**, 33 (1968).
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- (4) C. H. DePuy, W. C. Arney, Jr., and D. H. Gibson, *ibid.*, **90**, 1830 (1968).
- (5) S. J. Cristol, W. Y. Lim, and A. R. Dahl, *ibid.*, **92**, 4013 (1970).